

REMARKS

The May 6, 2005 Official Action and the references cited therein have been carefully reviewed. In view of the amendments presented herewith and the following remarks, favorable reconsideration and allowance of this application are respectfully requested.

At the outset, Applicants note that the Examiner has modified the restriction requirement and has agreed to examine Groups I, II and III in view of Applicant's remarks and claim amendments. Thus, claims 1-13 are currently being examined on the merits.

The Examiner has objected to the Information Disclosure Statement asserting that certain references were allegedly listed but not included. Applicants have reviewed copies of the IDS and PTO 1449 sent to the USPTO and both the Schaeffer and dos Santos references are present. It appears that these papers have been lost by the Patent Office. Accordingly, Applicants are submitting in a second paper a new PTO 1449 and Information Disclosure Statement requesting that these references be considered by the Examiner. Applicants do not believe a fee is due for this consideration as the initial IDS was properly filed and did contain these papers. The Examiner has also objected to the inclusion of GenBank printouts of AHSP sequences as they allegedly lack a publication date.

At page 7 of the Official Action, the Examiner has rejected claims 1-13 under 35 U.S.C. §112, first paragraph as allegedly failing to be enabled by the disclosure in the specification.

Claims 1-8 stand rejected under 35 U.S.C. §112, second paragraph as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter regarded as the invention. Specifically, the Examiner asserts that recitation of the term "harboring" renders the metes and

bounds of the claims unclear.

Claims 1-8 stand rejected under 35 U.S.C. §102(b) as allegedly anticipated by Kihm et al.

The Examiner has also rejected claims 9-13 under 35 U.S.C. §103(a) as allegedly obvious over Kihm et al. in view of Cappuccetti et al.

Applicants respectfully submit that the claims as presently amended are in condition for allowance. Each of the above-noted objections and rejections under 35 U.S.C. §112, first and second paragraphs, §102 and §103 is, therefore, respectfully traversed.

**THE SUBJECT MATTER OF CLAIMS 1-13 IS FULLY ENABLED BY THE
DISCLOSURE IN THE SPECIFICATION AS FILED**

The Examiner has rejected claims 1-13 under 35 U.S.C. §112, first paragraph for as allegedly failing to be enabled by the disclosure in the specification. Specifically, the Examiner contends that claim 1 appears to encompass a transgenic mice comprising a null mutation in its endogenous AHSP gene and an additional transgene. Applicants respectfully submit that the Examiner has misinterpreted the scope of claim 1 which is clearly drawn to an AHSP knock-out mouse.

A rejection under 35 U.S.C. §112, first paragraph, based on inadequate enablement is proper only when the rejected claim(s) is (are) of such breadth as to read on subject matter to which the specification is not enabling. In re Borkowski, 164 U.S.P.Q. 642 (CCPA 1970). Moreover, it is settled law that whenever the adequacy of enablement provided by an applicant's specification is challenged, the PTO has the initial burden of giving reasons, supported by the record as a whole, why the specification is not enabling. In re Armbruster, 185 U.S.P.Q. 152 (CCPA 1975). Indeed, a properly supported showing that the disclosure entails undue

experimentation is part of the PTO's initial burden under §112, first paragraph. In re Angstadt, 190 U.S.P.Q. 214 (CCPA 1976). Claim 1 as amended and claims dependent therefrom are clearly enabled by the disclosure provided in the application. Support for the amendment to claim 1 can be found at page 46 of the disclosure wherein the creation of the knock-out mice encompassed by the claims is described. The Examiner's remarks at page 14 regarding the fertility of the instantly claimed mice are unclear. Claim 2 states that the knock out mice of claim 1 are fertile and transmit the transgene to their offspring. This is proper dependent claim. It is submitted that the mice of claim 2 are fully described and enabled by the present specification. However, in order to expedite issuance of the present claims, claim 2 has been further amended to remove the phrase "is fertile and". It is submitted that this amendment obviates the Examiner concerns as to whether the mice encompassed by claim 1 are fertile or infertile. Claims 3 and 4 have also been amended to replace the phrase "null mutation" with "transgene". It is respectfully submitted that the skilled person is well aware of methods and compositions suitable for introducing a transgene into a blastocyst or embryonic stem cell.

Claim 5-8 have also been amended in a similar fashion to replace the phrase "null mutation" with "transgene". Again, the person skilled in the art of the creation of transgenic knock out mice is well aware of recombinant and breeding methods which result in the creation of knock-out mice that are either heterozygous or homozygous for the disrupted gene. Thus, it is submitted that these claims are also fully enabled by the disclosure in the specification.

The Examiner contends that the skilled person would not know how to use the mice of the invention in methods for screening therapeutics that affect AHSP using a mouse which comprises a null mutation of AHSP. Applicants respectfully

submit that the specification provides a number of different AHSP activities to assess in connection with the screening method encompassed by claim 9. Indeed as disclosed in the Figure legend for Figure 8 at page 12, erythrocytes isolated from the AHSP knockout mice of the invention exhibit abnormal morphology. The person of skill in this art, therefore could readily envision using the mice of the invention in screening methods for agents which restore the normal morphology of erythrocytes without having to resort to undue experimentation. New claim 39 has been included which specifically recites that the agent is assessed for its capacity to alter at least one characteristic selected from the group consisting of abnormal spiculated morphology, reduced lifespan, increased production of reactive oxygen species (ROS), and precipitated hemoglobin in erythrocytes obtained from the transgenic mice of the invention. The subject matter of this claim is supported by claim 1 and is fully enabled by the specification as filed.

At page 18 of the Official Action, the Examiner contends that claims 11-13 are not enabled by the disclosure in the specification. Specifically, it is the Examiner's position that since the mice do not exhibit alpha-thalassemia, beta-thalassemia, TSE or Alzheimer's disease, the claims are not enabled. Claim 11 has been amended to recite that the test agent is being assessed for its capacity to alter one or more characteristics selected from the group consisting of abnormal spiculated morphology, reduced lifespan, increased production of reactive oxygen species (ROS), and precipitated hemoglobin in the erythrocytes of said mouse. Claim 13 has been cancelled.

In light of all the foregoing remarks and claim amendments, it is respectfully submitted that the skilled person could readily practice the invention encompassed by these claims without resorting to undue experimentation.

Accordingly, the rejection of claims 1-13 under 35 U.S.C. §112, first paragraph based on inadequate enablement is untenable and should be withdrawn.

**THE METES AND BOUNDS OF CLAIMS 1-13 AS AMENDED ARE CLEAR TO
ONE OF ORDINARY SKILL IN THE ART**

The relevant inquiry in determining whether a given claim satisfies the requirements of 35 U.S.C. §112, second paragraph, is whether the claim sets out and circumscribes a particular area with a reasonable degree of precision and particularity such that the metes and bounds of the claimed invention are reasonably clear. In re Moore, 169 U.S.P.Q. 236 (CCPA 1971). Applicants respectfully submit that with respect to claims 1-13 of the present application, such inquiry must be answered in the affirmative.

As the Examiner acknowledges, the Merriam-Webster online dictionary defines the term "harboring" broadly as "containing". Accordingly, Applicants submit that the metes and bounds of the claims as filed are clear to one of ordinary skill in the art. However, in an effort to expedite prosecution in this case, the claims have been amended to recite transgenic mice wherein one or both alleles encoding Alpha Hemoglobin Stabilizing Protein (AHSP) have been disrupted via targeted insertion of a transgene. It is believed the present amendment serves to remove any perceived ambiguity from the claim. Accordingly, it is respectfully requested that the rejection of claims 1-13 as allegedly indefinite be withdrawn.

**A. CLAIMS 1-8 AS AMENDED ARE NOT ANTICIPATED BY THE
DISCLOSURE IN KIHM ET AL.; AND**

**B. CLAIMS 9-13 ARE NOT RENDERED OBVIOUS OVER THE COMBINED
DISCLOSURES OF KIHM ET AL. AND CAPECCHI ET AL.**

The Examiner has rejected claims 1-8 under 35 U.S.C. §102(a) as allegedly anticipated by Kihm et al. (2003).

Kihm et al. (2002) is not citable as prior art in the present case, as the law is well settled that one's own work is not prior art under §102(a) even though it has been disclosed to the public in a manner or form which otherwise would fall under §102(a). In re Katz, 215 U.S.P.Q. 14 (CCPA 1982). Consequently, Kihm et al. (2002) cannot support a rejection under 35 U.S.C. §103. Ex Parte Oetiker, 23 U.S.P.Q.2d 1641 (BPAI 1992).

The inventive entity on the present application has been amended under 37 C.F.R. 1.48 to include Dr. Kihm as a co-inventor. The papers supporting this amendment, i.e., the requisite newly executed Inventors' Declarations, Consent by the Assignee, Declaration by Dr. Kihm and fee are enclosed. Kihm et al. was published in June of 2002, less than a year prior to the priority date of the instant application which is June 12, 2003. The other co-authors listed on this manuscript (Wei Hong, J. Eric Russell, Susan Rouda, Kazuhiko Adachi, and M. Celeste Simon) are not co-inventors of the invention presently claimed in the present application.

Also attached hereto is a Declaration from Drs. Weiss, Kong, Kihm and Blobel averring that they are the co-inventors of the subject matter presently claimed. Unsigned Declarations from Dr. Yi Kong are currently being submitted. The undersigned is awaiting the executed Declarations from Dr. Yi Kong which will immediately be forwarded to the USPTO upon receipt thereof.

In light of the foregoing, it is clear that the rejections under 35 U.S.C. §§102 and 103 based on Kihm et al. or a combination of references comprising Kihm et al. are

improper and should be withdrawn.

CONCLUSION

The pending claims in this application are clearly in condition for allowance. Accordingly, it is respectfully urged that the rejections set forth in the May 6, 2005 Official Action be withdrawn and that this application be passed to issue. In the event the Examiner is not persuaded as to the allowability of any claim, and it appears that any outstanding issues may be resolved through a telephone interview, the Examiner is requested to telephone the undersigned attorney at the phone number given below.

Respectfully submitted,

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